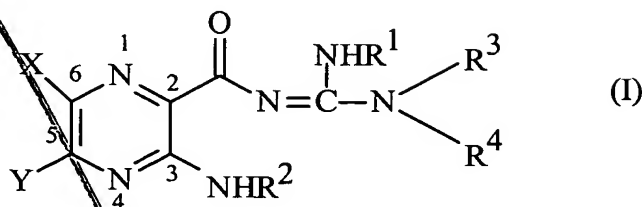


CLAIMS:

1. A compound represented by formula (I):



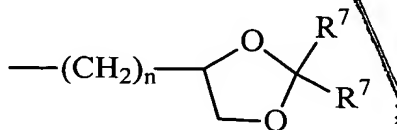
wherein

X is hydrogen, halogen, trifluoromethyl, lower alkyl, unsubstituted or substituted phenyl, lower alkyl-thio, phenyl-lower alkyl-thio, lower alkyl-sulfonyl, or phenyl-lower alkyl-sulfonyl;

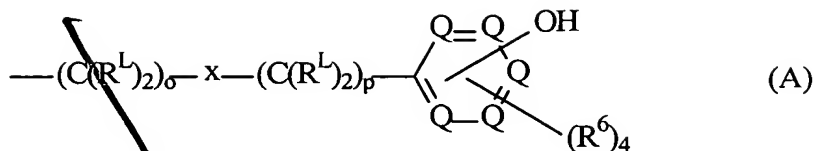
Y is hydrogen, hydroxyl, mercapto, lower alkoxy, lower alkyl-thio, halogen, lower alkyl, unsubstituted or substituted mononuclear aryl, or -N(R²)₂;

R¹ is hydrogen or lower alkyl;

each R² is, independently, -R⁷, -(CH₂)_m-OR⁸, -(CH₂)_m-NR⁷R¹⁰, -(CH₂)_n(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸, -(CH₂CH₂O)_m-R⁸, -(CH₂CH₂O)_m-CH₂CH₂NR⁷R¹⁰, -(CH₂)_n-C(=O)NR⁷R¹⁰, -(CH₂)_n-Z_g-R⁷, -(CH₂)_m-NR¹⁰-CH₂(CHOR⁸)(CHOR⁸)_n-CH₂OR⁸, -(CH₂)_n-CO₂R⁷, or

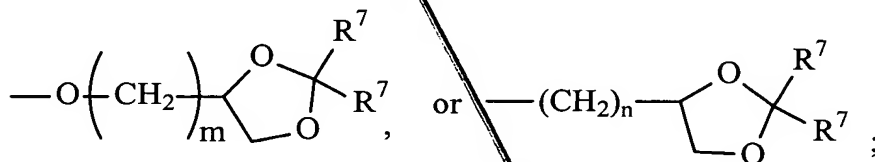


15 R³ and R⁴ are each, independently, hydrogen, a group represented by formula (A), lower alkyl, hydroxy lower alkyl, phenyl, phenyl-lower alkyl, (halophenyl)-lower alkyl, lower-(alkylphenylalkyl), lower alkoxyphenyl)-lower alkyl, naphthyl-lower alkyl, or pyridyl-lower alkyl, with the proviso that at least one of R³ and R⁴ is a group represented by formula (A):



wherein

each R^{L} is, independently, $-\text{R}^7$, $-(\text{CH}_2)_n-\text{OR}^8$, $-\text{O}-(\text{CH}_2)_m-\text{OR}^8$, $-(\text{CH}_2)_n-\text{NR}^7\text{R}^{10}$, $-\text{O}-(\text{CH}_2)_m-\text{NR}^7\text{R}^{10}$, $-(\text{CH}_2)_n(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$, $-\text{O}-(\text{CH}_2)_m(\text{CHOR}^8)(\text{CHOR}^8)_m-\text{CH}_2\text{OR}^8$, $-(\text{CH}_2\text{CH}_2\text{O})_m-\text{R}^8$, $-\text{O}-(\text{CH}_2\text{CH}_2\text{O})_m-\text{R}^8$, $-(\text{CH}_2\text{CH}_2\text{O})_m-\text{CH}_2\text{CH}_2\text{NR}^7\text{R}^{10}$, $-\text{O}-(\text{CH}_2\text{CH}_2\text{O})_m-\text{CH}_2\text{CH}_2\text{NR}^7\text{R}^{10}$, $-(\text{CH}_2)_n-\text{C}(=\text{O})\text{NR}^7\text{R}^{10}$, $-\text{O}-(\text{CH}_2)_m-\text{C}(=\text{O})\text{NR}^7\text{R}^{10}$, $-(\text{CH}_2)_n-(\text{Z})_g-\text{R}^7$, $-\text{O}-(\text{CH}_2)_m-(\text{Z})_g-\text{R}^7$, $-(\text{CH}_2)_n-\text{NR}^{10}-\text{CH}_2(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$, $-\text{O}-(\text{CH}_2)_m-\text{NR}^{10}-\text{CH}_2(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$, $-(\text{CH}_2)_n-\text{CO}_2\text{R}^7$, $-\text{O}-(\text{CH}_2)_m-\text{CO}_2\text{R}^7$, $-\text{OSO}_3\text{H}$, $-\text{O-glucuronide}$, $-\text{O-glucose}$, or



each x is, independently, O , NR^7 , $\text{C}=\text{O}$, CHOH , $\text{C}=\text{N}-\text{R}^6$, or represents a single bond;

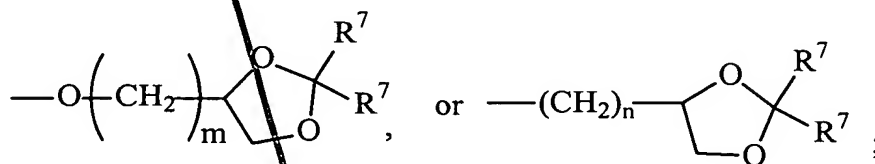
each o is, independently, an integer from 0 to 10;

each p is, independently, an integer from 0 to 10;

with the proviso that (a) the sum of o and p in each contiguous chain is from 1 to 10 when x is O , NR^7 , $\text{C}=\text{O}$, or $\text{C}=\text{N}-\text{R}^6$ or (b) that the sum of o and p in each contiguous chain is from 4 to 10 when x represents a single bond;

each R^6 is, independently, $-\text{R}^7$, $-\text{OH}$, $-\text{OR}^{11}$, $-\text{N}(\text{R}^7)_2$, $-(\text{CH}_2)_m-\text{OR}^8$, $-\text{O}-(\text{CH}_2)_m-\text{OR}^8$, $-(\text{CH}_2)_n-\text{NR}^7\text{R}^{10}$, $-\text{O}-(\text{CH}_2)_m-\text{NR}^7\text{R}^{10}$, $-(\text{CH}_2)_n(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$, $-\text{O}-(\text{CH}_2)_m(\text{CHOR}^8)(\text{CHOR}^8)_m-\text{CH}_2\text{OR}^8$, $-(\text{CH}_2\text{CH}_2\text{O})_m-\text{R}^8$, $-\text{O}-(\text{CH}_2\text{CH}_2\text{O})_m-\text{R}^8$, $-(\text{CH}_2\text{CH}_2\text{O})_m-\text{CH}_2\text{CH}_2\text{NR}^7\text{R}^{10}$, $-\text{O}-(\text{CH}_2\text{CH}_2\text{O})_m-\text{CH}_2\text{CH}_2\text{NR}^7\text{R}^{10}$, $-(\text{CH}_2)_n-\text{C}(=\text{O})\text{NR}^7\text{R}^{10}$,

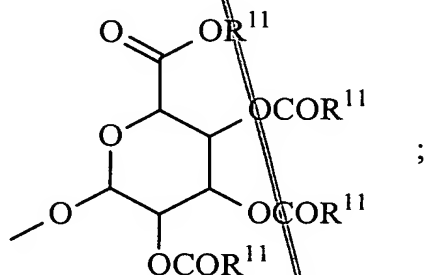
$-O-(CH_2)_m-C(=O)NR^7R^{10}, -(CH_2)_n-(Z)_g-R^7, -O-(CH_2)_m-(Z)_g-R^7,$
 $-(CH_2)_n-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8,$
 $-O-(CH_2)_m-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8,$
 $-(CH_2)_n-CO_2R^7, -O-(CH_2)_m-CO_2R^7, -OSO_3H, -O\text{-glucuronide}, -O\text{-glucose},$



wherein when two R^6 are $-OR^{11}$ and are located adjacent to each other on a phenyl ring, the alkyl moieties of the two R^6 may be bonded together to form a methylenedioxy group;

each R^7 is, independently, hydrogen or lower alkyl;

each R^8 is, independently, hydrogen, lower alkyl, $-C(=O)-R^{11}$, glucuronide, 2-tetrahydropyranyl, or



each R^9 is, independently, $-CO_2R^7$, $-CON(R^7)_2$, $-SO_2CH_3$, or $-C(=O)R^7$;

each R^{10} is, independently, $-H$, $-SO_2CH_3$, $-CO_2R^7$, $-C(=O)NR^7R^9$, $-C(=O)R^7$, or $-CH_2-(CHOH)_n-CH_2OH$;

each Z is, independently, $CHOH$, $C(=O)$, $CHNR^7R^{10}$, $C=NR^{10}$, or NR^{10} ;

each R^{11} is, independently, lower alkyl;

each g is, independently, an integer from 1 to 6;

each m is, independently, an integer from 1 to 7;

each n is, independently, an integer from 0 to 7;

each Q is, independently, $C-R^5$, $C-R^6$, or a nitrogen atom, wherein at most three Q in a ring are nitrogen atoms;

or a pharmaceutically acceptable salt thereof, and
inclusive of all enantiomers, diastereomers, and racemic mixtures thereof.

- 5
2. The compound of Claim 1, wherein Y is -NH_2 .
3. The compound of Claim 2, wherein R^2 is hydrogen.
4. The compound of Claim 3, wherein R^1 is hydrogen.
5. The compound of Claim 4, wherein X is chlorine.
6. The compound of Claim 5, wherein R^3 is hydrogen.
7. The compound of Claim 6, wherein each R^L is hydrogen.
8. The compound of Claim 7, wherein o is 4.
9. The compound of Claim 8, wherein p is 0.
10. The compound of Claim 9, wherein x represents a single bond.
11. The compound of Claim 10, wherein each R^6 is hydrogen.

12. The compound of Claim 11, wherein at most one Q is a nitrogen atom.

15

13. The compound of Claim 12, wherein no Q is a nitrogen atom.

20

14. The compound of Claim 1, wherein
X is halogen;
Y is $\text{-N(R}^7)_2$;
 R^1 is hydrogen or $\text{C}_1\text{-C}_3$ alkyl; and
 R^2 is -R^7 , $\text{-(CH}_2)_m\text{-OR}^7$, or $\text{-(CH}_2)_n\text{-CO}_2\text{R}^7$;

R^3 is a group represented by formula (A); and
 R^4 is hydrogen, a group represented by formula (A), or lower alkyl;

15. The compound of Claim 14, wherein

X is chloro or bromo;

Y is $-N(R^7)_2$;

R^2 is hydrogen or C_1 - C_3 alkyl;

at most three R^6 are other than hydrogen as defined above;

at most three R^L are other than hydrogen as defined above; and

at most 2 Q are nitrogen atoms.

16. The compound of Claim 15, wherein Y is $-NH_2$.

17. The compound of Claim 16, wherein

R^4 is hydrogen;

at most one R^L is other than hydrogen as defined above;

at most two R^6 are other than hydrogen as defined above; and

at most 1 Q is a nitrogen atom.

18. The compound of Claim 17, wherein x is O, NR^7 , $C=O$, $CHOH$, or $C=N-R^6$.

19. The compound of Claim 17, wherein x represents a single bond.

20. The compound of Claim 1, wherein x is O, NR^7 , $C=O$, $CHOH$, or $C=N-R^6$.

21. The compound of Claim 1, wherein x represents a single bond.

22. The compound of Claim 1, wherein each R^6 is hydrogen.

23. The compound of Claim 1, wherein at most two R^6 are other than hydrogen as defined in Claim 1.

24. The compound of Claim 1, wherein one R⁶ is other than hydrogen as defined in Claim 1.

25. The compound of Claim 1, wherein one R⁶ is -OH.

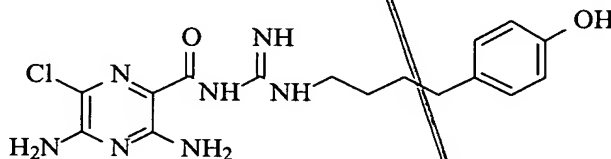
26. The compound of Claim 1, wherein each R^L is hydrogen.

27. The compound of Claim 1, wherein at most two R^L are other than hydrogen as defined in Claim 1.

28. The compound of Claim 1, wherein one R^L is other than hydrogen as defined in Claim 1.

29. The compound of Claim 1, wherein x represents a single bond and the sum of o and p is 4 to 6.

30. The compound of Claim 1, which is represented by the formula

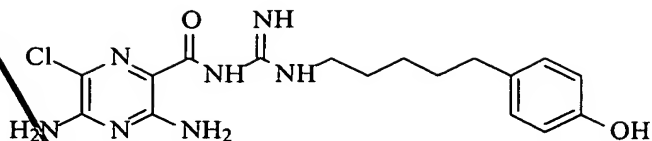


31. The compound of Claim 30, which is in the form of a pharmaceutically acceptable salt.

32. The compound of Claim 31, which is in the form of a hydrochloride salt.

33. The compound of Claim 1, which is represented by the formula

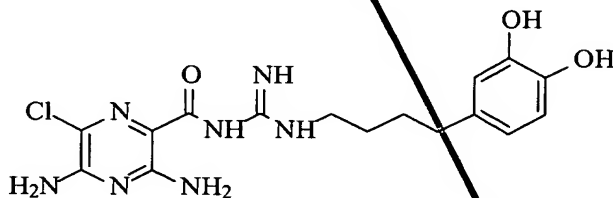
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34. The compound of Claim 33, which is in the form of a pharmaceutically acceptable salt.

35. The compound of Claim 34, which is in the form of a hydrochloride salt.

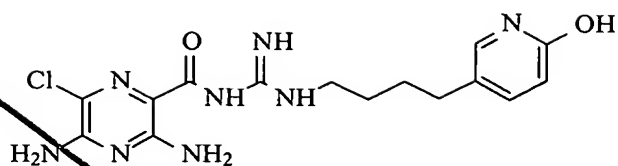
36. The compound of Claim 1, which is represented by the formula



37. The compound of Claim 36, which is in the form of a pharmaceutically acceptable salt.

38. The compound of Claim 37, which is in the form of a hydrochloride salt.

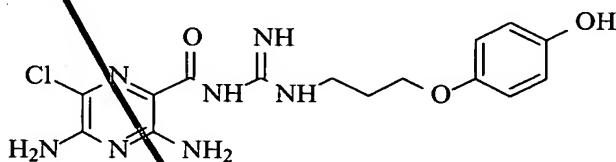
39. The compound of Claim 1, which is represented by the formula



40. The compound of Claim 39, which is in the form of a pharmaceutically acceptable salt.

41. The compound of Claim 40, which is in the form of a hydrochloride salt.

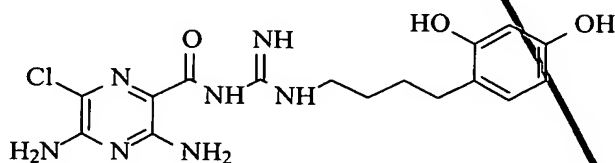
42. The compound of Claim 1, which is represented by the formula



43. The compound of Claim 42, which is in the form of a pharmaceutically acceptable salt.

44. The compound of Claim 43, which is in the form of a hydrochloride salt.

45. The compound of Claim 1, which is represented by the formula



46. The compound of Claim 45, which is in the form of a pharmaceutically acceptable salt.

47. The compound of Claim 46, which is in the form of a hydrochloride salt.

48. The compound of Claim 1, which is in the form of a pharmaceutically acceptable salt.

49. A pharmaceutical composition, comprising the compound of Claim 1 and a pharmaceutically acceptable carrier.

50. A method of promoting hydration of mucosal surfaces, comprising:
administering an effective amount of the compound of Claim 1 to a mucosal surface of a subject.

51. A method of restoring mucosal defense, comprising:
topically administering an effective amount of the compound of Claim 1 to a mucosal surface of a subject in need thereof.

52. A method of blocking sodium channels, comprising:
contacting sodium channels with an effective amount of the compound of Claim 1.

53. A method of treating chronic bronchitis, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

54. A method of treating cystic fibrosis, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

55. A method of treating sinusitis, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

56. A method of treating vaginal dryness, comprising:
administering an effective amount of the compound of Claim 1 to the vaginal tract of a subject in need thereof.

57. A method of treating dry eye, comprising:
administering an effective amount of the compound of Claim 1 to the eye of a subject in need thereof.

58. A method of promoting ocular hydration, comprising:
administering an effective amount of the compound of Claim 1 to the eye of a subject.

59. A method of promoting corneal hydration, comprising:
administering an effective amount of the compound of Claim 1 to the eye of a subject.

60. A method of promoting mucus clearance in mucosal surfaces, comprising:
administering an effective amount of the compound of Claim 1 to a mucosal surface of a subject.

61. A method of treating Sjogren's disease, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

62. A method of treating distal intestinal obstruction syndrome, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

63. A method of treating dry skin, comprising:
administering an effective amount of the compound of Claim 1 to the skin of a subject
in need thereof.

64. A method of treating esophagitis, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

65. A method of treating dry mouth (xerostomia), comprising:
administering an effective amount of the compound of Claim 1 to the mouth of a
subject in need thereof.

66. A method of treating nasal dehydration, comprising:
administering an effective amount of the compound of Claim 1 to the nasal passages
of a subject in need thereof.

67. The method of Claim 66, wherein the nasal dehydration is brought on by
administering dry oxygen to the subject.

68. A method of preventing ventilator-induced pneumonia, comprising:
administering an effective amount of the compound of Claim 1 to a subject on a
ventilator.

69. A method of treating asthma, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

70. A method of treating primary ciliary dyskinesia, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need
thereof.

71. A method of treating otitis media, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

72. A method of inducing sputum for diagnostic purposes, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

73. A method of treating chronic obstructive pulmonary disease, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

74. A method of treating emphysema, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

75. A method of treating pneumonia, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

76. A method of treating constipation, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

77. The method of Claim 76, wherein the compound is administered orally or via a suppository or enema.

78. A method of treating chronic diverticulitis, comprising:
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

79. The present invention also provides a method of treating rhinosinusitis, comprising:

administering an effective amount of the compound of Claim 1 to a subject in need thereof.

80. A composition, comprising:
the compound of Claim 1; and
a P2Y2 inhibitor.

81. A composition, comprising:
the compound of Claim 1; and
a bronchodilator.